University of California, San Francisco

Consent to Participate in a Research Study

For Adult Subjects, Parents/Legal Guardians, and Minor subjects 16 years of age - age of majority

Sponsor / Study Title	**AbbVie Inc. / "A Multicenter, Randomized, Double-Blind, Placebo-Controlled Induction Study to Evaluate the Efficacy and Safety of Risankizumab in Subjects with Moderately to Severely Active Ulcerative Colitis"**
Protocol Number:	**M16-067**
Principal Investigator: (Study Doctor)	**Kendall Beck, MD**
Telephone:	**415-514-8947** **415-502-4444 (24 Hours)**
Address:	**University of California, San Francisco** **1701 Divisadero Street, Suite 120** **San Francisco, CA 94115**

You are being asked whether you would like to voluntarily participate in a research study of a drug called Risankizumab. Your study doctor, Kendall Beck, MD, from the UCSF Department of Gastroenterology, will explain the study to you.

What is a research study?

A research study is an experiment whose purpose is to answer specific questions, such as:

- Does this drug work? Is it safe?
- What kind of treatment is better?

To answer these questions, doctors and scientists need volunteers to participate in research studies. These volunteers are called "subjects." The doctor in charge of the study at the study site is called the "study doctor" or "investigator". The study doctor and scientists who run the research study are called "researchers", and other people who help them run the study are called the "research team."

Advarra Institutional Review Board (IRB) has approved this study. The IRB is a group of people who review research studies to see if they meet federal laws and ethical standards. IRB approval only means it is ok for the study to begin. Only you can decide if being in this study is the right decision. Feel free to talk about this study with your family, friends and personal

doctor before you decide. We will answer any questions you may have so that you can make an informed decision.

The sponsor for this study is AbbVie. AbbVie pays the study site for the study doctor to run the study.

When reading this form, please note that the words "you" and "your" refer to the person in the study and not a parent, guardian or legally authorized representative who may sign this form on behalf of the person in the study.

Purpose of Study:

The purpose of this study is to evaluate the efficacy and safety of risankizumab and determine how well it works in subjects with moderate to severe ulcerative colitis.

You have been asked to participate in a research study of an investigational drug called risankizumab which is being studied to treat subjects with moderately to severely active ulcerative colitis. AbbVie is sponsoring this study. AbbVie is paying the study doctor to perform this study. An investigational drug is one that has not been approved by the regulatory authorities in your country (US Food and Drug Administration - FDA).
Risankizumab is made in the laboratory and is a monoclonal antibody which means is the same as a protein in your body, called an antibody. It works by blocking the actions of a protein known as Interleukin 23. Interleukin 23 is involved in the immune response and plays an important role in the development of chronic inflammation. Risankizumab is being studied in patients with inflammatory bowel disease and other inflammatory diseases.

You have been diagnosed with ulcerative colitis and are experiencing symptoms such as diarrhea with or without blood, abdominal pain, and may have a sudden or constant feeling that you need to move your bowels. Additionally, you may have been unable to tolerate or you may have had insufficient response to treatment with medications that help reduce the inflammation associated with your disease, such as mesalazine, corticosteroids, immunosuppressants and/or biologics (genetically-engineered proteins derived from human genes).

Study Information:

This study is being conducted at approximately 400 research centers worldwide and is expected to enroll 720 subjects in total with moderately to severely active ulcerative colitis.
Approximately 3 subjects will be enrolled at UCSF.
This study is divided into two sub-studies that will occur one after the other:

- Sub-study 1 (completed), was a dose-ranging induction sub-study. The aim of this sub-study was to determine the most appropriate dose of risankizumab to study further. Approximately 240 subjects participated in Sub-study 1. After these subjects were enrolled and completed the 12-week induction period, an analysis of the effectiveness and safety of risankizumab was performed. This analysis identified rizankizumab 1200

mg as the dose to be used for more evaluation in Sub-study 2. During the analysis period, 341 additional subjects were enrolled into Sub-study 1 until the risankizumab dose for Sub-study 2 was determined. Enrollment in Sub-study 1 is already completed.

- Sub-study 2, is a dose-confirming induction sub-study and has started once a dose of risankizumab has been selected from Sub-study 1. Approximately 966 subjects will participate in Sub-study 2.

The duration of the study and the number of visits to the site are the same, regardless which sub-study you participate in. Your participation in this study could be up to 45 weeks, including a Screening Period of up to 5 weeks and a 12-week double-blind (double blind means that neither you nor your study doctor will know which study drug or dose you receive) induction period (an induction period is the time from initial receipt of a medicine and to when a demonstrable response to the medicine is expected to be seen). The induction period will include approximately 4 study visits to the research center. If you have improved enough during the initial 12 week double-blind induction period you may be eligible to go into the maintenance study for risankizumab

If your disease has not improved enough with the initial study induction treatment, an additional 12-week double blind induction period may be undertaken, which will include approximately 3 study visits to the research center and a 140-day follow-up period if you do not continue into the maintenance study with risankizumab, or discontinue from the study prematurely. You may come in for additional unscheduled visits, as necessary.

If you decide to take part in the study, your study doctor will determine if you meet the study requirements and can enter the study. A daily electronic diary will be provided to you at the initial screening visit to assist in this evaluation and its completion is mandatory for the entire study. In order for your study doctor to confirm your eligibility at the beginning of the study and to evaluate how the drug is working throughout the study, it is critical that the diary be completed daily.

This study will use competitive enrollment. This means that when a target number of subjects begin the study, all further enrollments will be closed. Therefore, it is possible that you could be in the screening phase, ready to begin the study, and be discontinued without your consent if the target number of subjects has already entered the study.

At any time, you may withdraw from the study and end study participation prematurely, or your study doctor may discontinue your participation for any reason at any time.

AbbVie may terminate this study early, either in its entirety or at any study site, for reasonable cause provided that written notice is submitted in advance of the intended termination. The study doctor may also terminate the study at his/her site for reasonable cause, after providing written notice to AbbVie in advance of the intended termination. Advance notice is not

required by either party if the study is stopped due to safety concerns. If AbbVie terminates the study for safety reasons, AbbVie will immediately notify the study doctor by telephone and subsequently provide written instructions for study termination.

If you are finally enrolled in the study, you will be randomly assigned (by chance like the flip of a coin) to receive either risankizumab *or* placebo (inactive substance that looks like risankizumab). The investigational product (risankizumab) is the active ingredient and is given as a subcutaneous medication (administered under the skin) or an intravenous medication (infused in the vein), the infusion will last up to approximately 120 minutes.

Placebo is not a drug and it is not expected to have any chemical effects on your body and it is not designed to treat any disease or illness. It looks like the study drug to ensure subjects and the study staff cannot guess what you are actually taking. This allows the study scientists to make the best judgment on whether the study drug is having effects that are greater than are expected by chance alone.

Neither you nor your study doctor will be able to pick which study drug or dose you receive. In case of an emergency, your study doctor can find out this information.

If you are enrolled in the study you will participate in Sub-study 2 and you will be randomly assigned to one of the following two groups:

- Group 1 receives 1200 mg of risankizumab intravenously (through a vein) on study visits Weeks 0, 4 and 8.
- Group 2 receives placebo intravenously on study visits Weeks 0, 4 and 8.

You will have a 67% chance of receiving risankizumab for 8 weeks and a 33% chance of receiving placebo for 8 weeks.

In the case that after receiving the study induction treatment your ulcerative colitis has not improved enough according to your doctor's assessment (regardless of which sub-study you are participating in), you will be eligible to receive risankizumab treatment for an additional induction period, called induction period 2. For this second induction period there are 4 groups and you will be randomly assigned (by chance, like the flip of a coin) to groups 1, 2, or 3 if you previously received risankizumab during the initial induction period. During induction period 2 you will receive either risankizumab intravenously (in the vein) or subcutaneously (injected under the skin). In order for you and your study doctor to not know which treatment you are receiving each group will receive both a placebo and active treatment as follows:

- Group 1 in Period 2 receives 1200 mg of risankizumab intravenously (through a vein) on study visits Weeks 12, 16 and 20. This group receives placebo subcutaneously (under the skin) at Weeks 12 and 20.
- Group 2 in Period 2 receives 360 mg of risankizumab subcutaneously on study visits Weeks 12 and 20.This group receives placebo intravenously at Weeks 12, 16 and 20.
- Group 3 in Period 2 receives 180 mg of risankizumab subcutaneously on study visits Weeks 12 and 20. This group receives placebo intravenously at Weeks 12, 16 and 20.

- If you received IV placebo during the initial induction treatment you will be assigned, in a double blinded manner, meaning that neither you nor your doctor will know of your assignment, to group 4:

  Group 4 receives 1200 mg of risankizumab until the risankizumab dose is selected, and the risankizumab selected dose after that, intravenously (through a vein) on study visits Weeks 12, 16 and 20. This group receives placebo subcutaneously (under the skin) at Weeks 12 and 20.

Study Screening Procedures:

In order to determine if you are eligible to participate in the study you will complete the screening procedures (activities, tests and evaluations) described below and in the study activities table.

- Informed consent: You will sign and date a study specific IRB approved Informed Consent Form
- Inclusion/Exclusion criteria
- Medical/Surgical History – including questions regarding tobacco, alcohol and drug use
- Physical Exam
- Review of any medications you are taking
- Vital Signs (blood pressure, heart rate, respiratory rate, and temperature) as well as height and weight
- ECG (a test which records the electrical activity of your heart)
- Endoscopy: During an endoscopy, you may be mildly sedated and a thin, flexible, lighted tube will be inserted inside the bowel. This will allow the doctor to look for abnormal areas. A biopsy will be taken during this test. Your doctor will examine your entire large bowel (colonoscopy) unless you have already had this performed in the previous 12 months, in which case they may decide to just examine the lower part of your large bowel (flexible sigmoidoscopy).
- Endoscopic biopsy: An endoscope is a long thin tube with lights that can be passed into the bowel. To perform a biopsy, a small clamp takes a small piece of superficial tissue from an area seen through the tube.
- Blood and Urine Testing: Blood and urine will be taken to do laboratory tests. For the blood assessments up to 24 ml (5 Teaspoons) will be drawn.
  - Blood test for hepatitis B and C - Positive hepatitis test results may be reportable to local public health department according to local laws, if applicable. You may have to sign a separate consent form before hepatitis testing can start.
  - Blood test for HIV: You will not be eligible for study participation if test results indicate HIV infection. Positive HIV test results may be reportable to local public health department according to local laws, if applicable.

  - FSH test, if you are female and younger than age 55, to determine if you have completed menopause.
- Pregnancy Testing: Test your blood and/or urine to see if you are pregnant. You will only have pregnancy testing if you are a woman and able to become pregnant.
  - The study doctor or study staff will tell you if the pregnancy test results are positive.
  - The results of the pregnancy testing must be negative in order for you to be in the study.
- PPD Skin Test or QuantiFERON-TB Gold Test (or IGRA equivalent such as T-SPOT) or both according to local guidelines to check for tuberculosis. If latent (existing but not active infection yet developed) tuberculosis is established TB prophylaxis/treatment should be initiated and maintained according to local country guidelines. Positive TB test results may be reportable to local public health department according to local laws, if applicable.
- X-ray: There is the possibility that your doctor will request an X-ray, for example, if you have a positive TB test or if required by local law.
- Stool samples: you will be required to provide a stool sample for laboratory test
- Dispense Subject Electronic Diary: The study site personnel will give you the study electronic diaries and tell you how to use them. You should bring the completed electronic diary back to the study center at each visit.

Study Procedures:

If you are eligible to participate in this study, you will undergo one or more of the study procedures described in this form at each study visit as described below and in the study activities table.

- Blood Testing: Blood will be taken to do laboratory tests. For the blood assessments approximately 8.5 - 10.5 ml (approximately 1-2 teaspoons) of blood will be drawn at each visit depending on the visit.
  - For the assessment of your blood cells, chemistry (such as glucose, kidney function and lipids), and the assessment of the degree of inflammation in your body (every visit) approximately 5.5mL (approximately 1 teaspoon) of blood will be drawn at dedicated visits.
  - For the assessment of the concentration of risankizumab (PK) levels in your blood approximately 2mL (0.5 teaspoon) of blood will be drawn at dedicated visits.
  - For the assessment of anti-drug antibodies (ADA) levels and assessment of neutralizing antibody (nAb) (antibodies that can block the effects of the study drug) levels in your blood approximately 3mL (0.5 teaspoon) of blood will be drawn at dedicated visits for each assessment.
  - Additionally, you may need additional blood tests and to return to the study site for some follow up testing or retesting that will collect approximately 11.5 mL (approximately 2.5 teaspoons) of blood to follow up any abnormal laboratory

test or if your study doctor feels you may be experiencing a suspected allergic reaction. Your study doctor may also request other tests, as part of your immediate medical care.

- Vital Signs (blood pressure, heart rate, respiratory rate, and temperature), and weight, with your height being measured at the baseline visit
- Physical Exam
- Review of any medications you are taking
- Endoscopy at visit Week 12 and also at visit Week 24 if you are in induction period 2. Biopsies will be done when performing the endoscopies. All endoscopy procedures (including biopsy) will be video recorded. Your doctor will decide if they need to examine your entire colon (colonoscopy) or just the bottom part (flexible sigmoidoscopy).
- Pregnancy Testing: Test your blood and/or urine to see if you are pregnant. You will only have pregnancy testing if you are a woman and can become pregnant. The study doctor or study staff will tell you if the pregnancy test results are positive. The results of the pregnancy testing must be negative in order for you to continue in the study.
- Stool samples: you will be required to provide a stool sample for laboratory test
- Urine samples: you will be required to provide urine samples for laboratory tests
- Electronic Questionnaires: Instead of using paper and pencil to understand your disease and your response to study drugs, an electronic diary device will be used to collect your answers to questions regarding your health. This device meets all regulations for use in clinical studies, including those related to your privacy. Your answers to these questions will be transferred to a storage facility via a secure internet connection and will be viewed by site and AbbVie.
- Review Subject Electronic Diary: You should bring the completed electronic diary back to the study center at each visit.
- Study drug administration

Subject Responsibilities:

In order for this study to provide good information about how the study drug works in subjects with your condition, you will be expected to do the following:

- Attend all study visits
- Tell the study doctor if you are feeling bad or worse than before
- Not change your basic treatment for ulcerative colitis before discussing it with the doctor
- Tell the study doctor if you have any changes in any medications during the study
- Follow the directions of the study doctor and research team
- Refrain from participation in other research studies while you are subject in this study

- Fill out the electronic questionnaires and electronic diary completely and honestly and bring the electronic diary to the study doctor's office at each visit
- Carry your subject card with you as long as you are in the study and show it to any medical staff that may be involved in your healthcare.
- Study location: All study procedures will be done at Gastroenterology Faculty Practice at 1701 Divisadero Street, Suite 120, San Francisco, CA 9415

Risks related to Study Procedures:

- Blood Draw for blood testing (including QuantiFERON test or T-SPOT TB to test for TB infection and serum pregnancy testing): Blood draws may cause pain, bleeding, and/or bruising. You may feel faint or pass out. There is a risk of bleeding or bruising at the puncture site and/or development of a small scar or an infection with redness and irritation of the vein at the site where blood is drawn. Frequent blood collection may cause anemia (low red blood cell count), which may create a need for blood transfusions.
- Electrocardiogram (ECG): Skin irritation is rare but could occur during an ECG from the electrodes or gel that is used. To do the ECG, you will have pads placed on different parts of your body. There is no pain or discomfort during an ECG; however, removing the pads may cause some irritation to your skin.
- Physical Exam: There are no special risks with an exam. It will be similar to examinations you have had in your doctor's office in the past.
- Serum Pregnancy Testing: the risks are similar to any blood test.
- Intravenous infusion of risankizumab or placebo: a thin needle is placed inside the vein and could cause similar risks to the ones described in the blood draw in addition to allergic and infusion related reactions (reactions that can happen when medicine is infused in your vein) as described below in the risankizumab risks.
- Subcutaneous Injection of risankizumab or placebo: a needle is used to inject the study drug or placebo under the skin. This can cause skin irritation and/or itching.
- Placebo: a placebo is not designed to have any chemical effects on your body. No risks are expected from a placebo. There may still be risks associated with other study procedures though.
- PPD test (to test for TB infection) - there may be slight discomfort where injection is administered. Rarely people can have a larger skin reaction at the site. This may require treatment for a couple of days.
- X-ray: You may have an X-Ray to check your lungs for TB infection: There can be risks of radiation from the X-ray. If X-Rays are needed, you will be exposed to a small amount of radiation, which is not considered significant. Please ask the study doctor or study staff if you have questions about the risks of the study procedures.
- Endoscopy/ Biopsy: Colonoscopy (which examines your entire colon), sigmoidoscopy (which examines only a portion of the colon) and biopsy of the colon are standard and commonly performed medical procedures to examine the large bowel. Your doctor will decide how much of your bowel they need to examine but both procedures may involve

some pain and discomfort. When a biopsy (removal of a small piece of tissue) is performed during the endoscopy, bleeding from the biopsy site may occur and you may see a small amount of blood in your stools. Other complications that may occur include infection at the biopsy site and bacteria in the blood. Rare complications of endoscopy with or without biopsy include tearing of the colon and/or bleeding and the rare occurrence of bowel perforation (creation of a hole in the bowel) and/or bleeding. These rare complications might require surgery and/or the use of antibiotics. You will be asked to sign a separate consent for the colonoscopy or sigmoidoscopy. If sedation is to be given for the procedure, your study doctor will discuss with you the risks of sedation. You will not be permitted to drive immediately after the procedure and, therefore, will need someone to drive you home.

- Fasting for up to 8 hours could cause dizziness, headache, stomach discomfort, or fainting.

Study Activities Table

		12-Week-Double-Blind Induction				12-Week Induction Period 2					
Study Activity	Screening	Baseline	Week 4	Week 8	Week 12	Week 16	Week 20	Week 24	Premature D/C	Unscheduled Visit	140 Day Follow-up[d]
Informed Consent	X										
Inclusion/Exclusion criteria	X	X									
Medical and Surgical History - including questions regarding tobacco, alcohol and drug use	X	X									
Vital Signs blood pressure, heart rate, respiratory rate and temperature, **Weight and Height**[a]	X	X	X	X	X	X	X	X	X	X	
Physical Exam	X	X	X	X	X	X	X	X	X	X	
ECG (a test which records the electrical activity of your heart)	X										
Endoscopy/Biopsy[b]	X				X			X	X[b]		
TB Screening	X										
Blood[c] **Tests** to monitor your health	X	X	X	X	X	X	X	X	X		
Urine Tests to monitor your health	X	X			X			X	X		
Hepatitis B and Hepatitis C Screening	X										
HIV testing	X										

		12-Week-Double-Blind Induction				12-Week Induction Period 2					
Study Activity	Screening	Baseline	Week 4	Week 8	Week 12	Week 16	Week 20	Week 24	Premature D/C	Unscheduled Visit	140 Day Follow-up[d]
Blood Test for the assessment of risankizumab (PK) levels in your blood			X	X	X			X	X	X	
Blood Test for the assessment of anti-drug antibody (ADA) and Neutralizing Anti-Drug Antibodies (nAb) levels in your blood		X	X	X	X			X	X	X	
Stool samples	X	X	X		X			X	X		
Pregnancy Test [e] serum and/or urine) (only for females who are able to get pregnant)	X	X	X	X	X	X	X	X	X	X	
FSH Blood Test (only for females if you are female and younger than 55 years old)	X										
Prior and Concomitant Medication Assessment (review of any other medication you are taking)	X	X	X	X	X	X	X	X	X	X	
Adverse Event Assessment (review of any side effects you are experiencing, which may or may not be related to the study drug)	X	X	X	X	X	X	X	X	X	X	X
Electronic Questionnaires		X	X	X	X	X	X	X	X	X	

		12-Week-Double-Blind Induction				12-Week Induction Period 2					
Study Activity	Screening	Baseline	Week 4	Week 8	Week 12	Week 16	Week 20	Week 24	Premature D/C	Unscheduled Visit	140 Day Follow-up[d]
Study Drugs Dispensing/ Administration[f]		X	X	X	X	X	X				
Daily diary review	X	X	X	X	X	X	X	X	X	X	

a.

Optional samples (only for subjects consenting optional exploratory sub-study)											
Study Activity	Screening	Baseline	Week 4	Week 8	Week12	Week 16	Week 20	Week 24	Premature D/C	Unscheduled Visit	140 Day Follow-up[d]
Optional Blood Samples		X			X			X	X		
Optional Tissue Samples	X				X			X	X		

D/C = Discontinuation

Please note that you may be asked to repeat a procedure or test if your study doctor feels it is needed to evaluate your condition.

a. Height will be measured at screening only.
b. You will undergo an endoscopy with biopsy during Screening and Week 12 visit. If you enter into induction period 2, you will undergo an additional endoscopy at Week 24. If you prematurely discontinue the study after Week 8, you will undergo an endoscopy at your discontinuation visit.
c. For some of the blood samples it is preferable to be collected while patients are in fasting condition.
d. You will be contacted 140 days following study drug discontinuation for an assessment of any new or ongoing adverse events, except if you roll over into risankizumab maintenance study M16-066. During this follow-up call you will be asked to communicate the results of the follow-up at home pregnancy test.
e. A serum pregnancy test will be performed on all women of childbearing potential at Screening. Urine pregnancy test will be performed at the site at Baseline all subsequent visits for all women of child bearing potential. If any urine pregnancy test is positive, a serum pregnancy test will be performed at the site and sent to the central laboratory. If a pregnancy is identified, the pregnancy must be reported to AbbVie
f. Study drug will be administered intravenously (through a vein) during your site visits at Baseline, Week 4 and Week 8 , after all assessments and examinations scheduled for that day have been completed. Study drug will only be administered at week 12 if you enter induction period 2. Study drug administration at week 12, Week 16 and Week 20 will be intravenously and

subcutaneously (under the skin). In the event of an anaphylactic reaction, or other suspected systemic hypersensitivity reaction, blood samples will be drawn 1 hour, 3 hours and 24 hours after the onset of the reaction for assessment.

g. If your doctor suspects the possibility of COVID-19 based on the signs, symptoms and medical complaint (chief complaint, history of exposure, etc.), local laboratory testing must be completed to confirm that you are negative for infection.

Study Drug Risks:

Risankizumab has been given to healthy volunteers and patients with psoriasis, erythrodermic psoriasis, generalized pustular psoriasis, psoriatic arthritis, Crohn's disease, ulcerative colitis, ankylosing spondylitis, asthma, atopic dermatitis, and hidradenitis suppurativa. Risankizumab has been given either by intravenous infusion (IV, slowly injected into a vein in the arm) or by subcutaneous injection (SC, injection into the deepest skin layer). It has been tested in repeated doses as high as 1800mg IV and 360 mg SC. No new or different side effects were seen with higher doses of risankizumab.

As of 25 March 2020, safety data were available for approximately 6242 subjects in both completed and ongoing studies, including 3072 with plaque psoriasis, 805 with psoriatic arthritis, 1064 with Crohn's disease, 111 with atopic dermatitis, 68 with hidradenitis suppurativa and 468 with ulcerative colitis.

Over 3000 people with psoriasis have been treated with risankizumab SC, predominantly with 150 mg dose. The rates of overall side effects and serious side effects were similar between risankizumab treatment and placebo treatment (an inactive substance). No new safety risks have been observed with risankizumab compared to the other antibody treatments that affect the immune system and were investigated in the risankizumab clinical development. In clinical trials that compared risankizumab to placebo and either ustekinumab or adalimumab, serious side effects occurred in 2.4% for the risankizumab group compared to 4.0% for the placebo group, and 5.0% for the ustekinumab group and 3.0% for the adalimumab group.

In a Phase 2 completed psoriatic arthritis study, 185 people received either 75 mg or 150 mg of risankizumab SC or placebo. The most frequent side effects reported in subjects who received risankizumab were viral upper respiratory tract infection (common cold caused by a virus) (17.5%), upper respiratory tract infection (common cold) (5.6%), and headache (5.6%).

In a Phase 2 completed Crohn's disease study, 121 subjects received 200 mg or 600 mg risankizumab or placebo by IV. Overall, the number of subjects who reported side effects was similar between subjects treated with risankizumab and subjects treated with placebo. The most frequently reported side effects (greater than 5% of subjects) in the risankizumab treatment group were arthralgia (joint pain) (17.1%), nausea (15.9%), headache (13.4%), abdominal pain (12.2%), asthenia (lack of energy) (7.3%), pyrexia (fever) (7.3%), vomiting (7.3%), and diarrhea (6.1%).

In the Phase 2 completed portion of this ulcerative colitis study, 240 subjects received 600, 1200 or 1800 mg doses of risankizumab or placebo IV. The most frequently reported side effects (greater than or equal to 3% of subjects receiving risankizumab) are nasopharyngitis (sore throat) (6.1%), headache (5%), nausea and ulcerative colitis (3.3% each). These rates were similar as in subjects receiving placebo.

Based on review of all the safety information to date, the following are known risks with risankizumab use:

Very common (greater than 10%): may affect more than 1 in 10 people

- Upper respiratory infections with symptoms such as sore throat and stuffy nose (13%)

Common (greater than 1% and less than 10%): may affect up to 1 in 10 people

- Feeling tired (2.5%)
- Fungal skin infection (1.1%)
- Injection site reactions (1.5%)
- Headache (3.5%)

Uncommon (less than 0.1% and greater than 1%): may affect up to 1 in 100 people

- Infection of hair follicles (seen as small raised red bumps on the skin)

Areas of Safety Interest

Infections: Risankizumab therapy is associated with an increased risk of infection. Serious infections leading to hospitalization have been reported in patients receiving risankizumab. Drugs that affect the body's immune system may increase the risk of infections, including tuberculosis (TB). You will be screened for signs of active infection before you start on risankizumab. Talk to your study doctor before and during use of risankizumab if you:

- Currently have an infection or if you have an infection that keeps coming back
- Have TB
- Have recently received or plan to receive an immunization (vaccine). You should not be given certain types of vaccines while using risankizumab

Injection Site Reactions: Injection of study drug under the skin could result in redness, pain, swelling or hardness at the site of the injection. Also, bleeding or bruising at the injection site may occur. Most injection site reactions are not severe and resolve without any treatment but can be uncomfortable for a few hours to a few days.

Other Possible Risks

Some drugs that affect the immune response have been associated with side effects such as serious allergic reactions, and possible increased risk of malignancy (cancer). These events have not been found associated with risankizumab.

Allergic Reactions: All drugs have a potential risk of an allergic reaction. Allergic reactions may vary from mild (rash, hives, itching) to severe reactions such as anaphylaxis (which may include difficulty breathing, swelling of the face or throat, low blood pressure, or loss of consciousness). A severe allergic reaction requires immediate medical treatment and could result in permanent disability or death. It is important to tell your study doctor about any past allergic reactions that you may have had to other drugs including antibody drugs (which are usually given by IV or injection under the skin). If you seek medical care for a possible allergic reaction, please request the treating health care provider to contact the study physician.

Infusion Reactions: Giving study drug by IV may result in an infusion-related reaction with symptoms such as fever, flushing of the skin, itching, rash or a decrease in blood pressure. If you are receiving study drug by IV, your study doctor will monitor for signs of an adverse reaction during the infusion.

Malignancy (cancer): When an immune system pathway is blocked, there is a possibility of a decreased immune defense against malignancies. In the completed studies to date, risankizumab has not been associated with an increased risk of malignancies but the risk with long term therapy is not known.

Cardiovascular Events**:** Subjects with inflammatory diseases such as psoriasis, psoriatic arthritis and inflammatory bowel disease have an, increased risks of major cardiovascular events (such as heart attacks, strokes or cardiovascular death) In the completed psoriasis studies to date, risankizumab has not shown an increased risk of these events. However, any new or worsening signs or symptoms such as chest, neck or arm pain, shortness of breath, sensation of rapid heart rate, new visual symptoms or muscle weakness should be immediately reported to your study site and/or primary health care provider.

There is no antidote to risankizumab. Any side effects occurring as a result of risankizumab will be treated symptomatically.

Pregnancy risks, risk to nursing infant and contraceptive precautions

You should not become pregnant or breastfeed a baby while on this study because it is not known if risankizumab is safe for a pregnant woman, an unborn baby and infant or child who are nursing. . It is important to understand that you need to use birth control while on this study. Check with your study doctor about what kind of birth control methods to us. Some methods might not be approved for use in this study. You must use birth control during study participation and 20 weeks after your last dose of study drug.

Effective methods of contraception acceptable to use during this study are:

- combined (estrogen and progestogen containing) hormonal birth control (oral, intravaginal, transdermal) associated with inhibition of ovulation, must start at least 1 month prior to study
- Progestogen-only hormonal birth control (oral, injectable, and implantable) associated with inhibition of ovulation, (must start at least 1 month prior to study)
- Bilateral tubal occlusion/ligation (can be via hysteroscopy, provided a hysterosalpingogram confirms success of the procedure)
- intrauterine device (IUD)
- intrauterine hormone-releasing system (IUS).
- vasectomized sexual partner(s) (the vasectomized partner should have received medical assessment of the surgical success and is the sole sexual partner of the trial participant)

- true abstinence: Refraining from heterosexual intercourse when this is in line with the preferred and usual lifestyle of the subject (periodic abstinence [for example, calendar, ovulation, symptothermal, post-ovulation methods] and withdrawal are not acceptable).

Some methods of birth control will not work when you are taking certain drugs. If you decide to take part in this study and you are able to become pregnant, a pregnancy test will be done before your participation in the study and regularly at some trial visits and at the end of the trial.

Once you're enrolled in the study, if you become pregnant or think you could be pregnant or are trying to get pregnant, it is important for you to tell the study doctor or staff immediately. If you become pregnant during the study, you will no longer receive study drug. Even if you are no longer in the study or not receiving study drug, your study doctor will contact you about your pregnancy and the outcome of the pregnancy

You also may take part in this clinical study if you are surgically sterilized (both ovaries or fallopian tubes removed or uterus removed) or you are post-menopausal (no menses for at least 1 year without other cause identified).

Unknown Risks

You may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. However, doctors do not know all the side effects that may happen. Side effects may be mild or very serious. Your health care team may give you medicines to help lessen side effects.

You may experience side effects that are not listed in this informed consent. As with any investigational drug, administration of risankizumab may involve risks that are currently unknown, including life threatening reactions or the remote possibility of death.

You should notify the study doctor of any changes in your health or new symptoms you are experiencing, even if you think these changes are not related to study drug.

You will be told of important new information about this study or the study drug that becomes available and that may affect your willingness to participate in this study.

SAFETY MONITORING

Blood tests to check your numbers of white, red blood cells and platelets will be done throughout the study. Blood levels of lipids (such as cholesterol), kidney function and liver function will be conducted. Measurements of heart rate and blood pressure will be checked throughout the study and electrocardiograms (looking at the electrical conduction of the heart) will be done. Physical examinations including checking your lymph nodes will be performed.

Tell your study doctor if you develop any signs of infection including fever, sweats, chills, flu-like symptoms, cough, shortness of breath, feeling very tired, diarrhea, skin rashes or sores, burning when you urinate, or urinating more often than normal.

Benefits:

You may or may not benefit from being in this study but your participation in this research study may benefit future patients with your disease or condition. Your condition may get better, it may get worse, or it may stay the same.

Alternatives to Participation:

You do not have to participate in this study to get help for your condition.
Your other choices may include:

- Getting standard treatment for your condition without being in a study. Other treatments commonly used for UC include: aminosalicylates (commonly known as 5-ASA – Asacol, Rowasa, and Pentasa); corticosteroids, immunosuppressants (examples include azathioprine [Imuran], mercaptopurine and methotrexate [Trexall, and Rheumatrex]; biologics (examples include: TNF blockers, infliximab [Remicade], adalimumab [Humira]) and golimumab [Simponi]; integrin receptor antagonist:
  vedolizumab [Entyvio]; surgery
- Taking part in another study.
- Getting no treatment.

Your study doctor can discuss the risks and advantages of these alternative treatment methods with you.

HIV/AIDS/HEPATITIS/TB Testing:

Depending on the local laws, you may have to sign a separate consent form before HIV testing can start. The study doctor or study staff will tell you if the results are positive. If required, the study doctor or study staff may report a positive test result to the local health department. Your study doctor will discuss with you what the local laws require with regard to reporting the test results.

Being tested for HIV may cause anxiety regardless of the test results. A positive test indicates that you have been infected with the HIV virus. If you test positive we will refer you to a source of medical care and treatment. Receiving positive results may make you very upset. If other people learn about your positive test results, you may face discrimination. If your test is negative, there is still the possibility that you could be infected with the HIV virus and test positive at some time in the future.

Positive results for HIV must be reported to a local health agency. This is the legal obligation of health professionals in this state. Based on state law or clinic policy, you may be asked to sign a separate HIV consent form.

Costs

Neither you nor your insurance company will have to pay for the study drug (or placebo) or procedures that are done only for the study. The sponsor will provide the drug risankizumab and administration of drug risankizumab at no cost to you.

Reimbursement and Payments

You will not be compensated for your participation in this study.

The sponsor and people or companies working with the sponsor may use your biological samples when developing new tests, procedures and commercial products. If this happens, the sponsor does not plan to share any profits with you.

Research Related Injuries

If you are injured as a result of being in this study, the University of California will provide necessary medical treatment. The costs of the treatment may be billed to you or your insurer just like any other medical costs, or covered by the University of California or the study sponsor AbbVie, depending on a number of factors. The University and the study sponsor do not normally provide any other form of compensation for injury. For further information about this, you may call the office of the Committee on Human Research at 415- 476-1814.AbbVie makes no commitment to provide compensation except as described above. You will not lose any of your legal rights or release the Sponsor, the study doctor, the study staff, or study site from liability for mistakes or intentional misconduct by signing this consent document.

What are my rights if I take part in this study?

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your medical care from our institution.

We will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

WHOM TO CONTACT ABOUT THIS STUDY

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study, please contact the Investigator , Kendall Beck, MD, at 415-502-4444.. If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research subjects. If you have any questions about your rights as a research subject, and/or concerns or complaints regarding this research study, contact**:**

- By mail:
  Study Subject Adviser
  Advarra IRB
  6940 Columbia Gateway Drive, Suite 110
  Columbia, MD 21046
- or call **toll free**: 877-992-4724
- or by **email**: adviser@advarra.com

Please reference the following number when contacting the Study Subject Adviser: Pro00025653.

INFORMATION ABOUT CONFIDENTIALITY

The study doctor, the sponsor or persons working on behalf of the sponsor, and under certain circumstances, the United States Food and Drug Administration (FDA) and the Institutional Review Board (IRB) will be able to inspect and copy confidential study-related records which identify you by name. This means that absolute confidentiality cannot be guaranteed. If the results of this study are published or presented at meetings, you will not be identified.

Participation in research involves some loss of privacy. We will do our best to make sure that information about you is kept confidential, but we cannot guarantee total privacy. Some information from your medical records will be collected and used for this study. If you do not have a UCSF medical record, one will be created for you. Your signed consent form and some of your research tests will be added to your UCSF medical record. Therefore, people involved with your future care and insurance may become aware of your participation and of any information added to your medical record as a result of your participation. Study tests that are performed by research labs, and information gathered directly from you by the researchers will be part of your research records but will not be added to your medical record. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

Can I see my records?

You may have the right to see and get a copy of your medical records. However, by signing this informed consent, you agree that you may not get to see your records relating to the study until after the study is over.

The optional research is exploratory in nature and cannot help your doctor or the investigator treat your disease. For this reason, you may not get the results of any testing that is done as part of that research, and the test results may not be put in your medical records.

A description of this clinical trial will be available on *http://www.ClinicalTrials.gov*, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Voluntary Participation and Withdrawal

You can decide to stop at any time. Tell the study doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop your participation safely.
It is important to tell the study doctor if you are thinking about stopping so any risks from the study can be evaluated by your doctor. Another reason to tell your doctor that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you.

The study doctor may stop you from taking part in this study at any time if he/she believes it is in your best interest, if you do not follow the study rules, or if the study is stopped.If AbbVie and/or other researchers collected any personal health information or did any testing before your withdrawal, AbbVie will still use the test results and keep the data generated from your samples. Additionally, if you take back your permission to use or disclose your personal information, you will be withdrawn from the optional research.

If you withdraw from the main study, your samples will continue to be stored and analyzed as described in this form unless you let the investigator know that you would like to withdraw consent for the research on your samples. Once AbbVie is notified that you have changed your mind, no new research will be started, and your samples will be destroyed unless the FDA requires the sponsor to keep the samples. However, data and results that are generated from testing on your samples before the sponsor is notified will still be used.

The main study and optional research may be stopped early by AbbVie, the investigator, the IRB or the FDA. You could be withdrawn from the main study or optional research without your consent, at any time and for any reason.

CONSENT

For Research Subjects in California: Before you sign this informed consent/authorization, you should read and sign a copy of the California Experimental Subject's Bill of Rights. Ask the study staff or the Investigator for a copy of this document if you have not already received one.

You will be asked to sign a separate form authorizing access, use, creation, or disclosure of health information about you.

Adult Subject name: _____

- I have read this form and the research study has been explained to me. I have been given the chance to ask questions, and my questions have been answered.
- I will receive a copy of this consent form after I sign it.
- I am not giving up any of my legal rights by signing this form.
- I agree to participate in the research study described above.

_____

Adult Subject signature Date Time

_____

Name of Person Conducting Informed Consent Discussion (Printed)

_____ _____

Signature of Person Conducting Informed Consent Discussion Date